REMARKS/ARGUMENTS

Claims 9-29 are pending. No amendment to the specification or claims is made in the present response. Reconsideration of the present application in view of the following remarks/arguments is respectfully requested.

Claims 9-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. Specifically, the Examiner states that the specification of the present application does not teach how to use a transgenic mouse as recited in the claims. Applicants disagree.

As specifically discussed in the present specification, the present invention utilizes the combination of mouse coat color genes and chicken insulators in transgenic mouse production to enhance transgene expression rate and characterize the genotype visually with coat color change when expressing transgene of interest on a mouse. See, e.g., paragraphs 0004-0006, 0013, 0015-0016, Examples 1-2. As discussed in the specification, functional genetics analysis, the techniques of genetic modifications in accordance with the prior art are time consuming and laborious, especially in mouse system (see, e.g., paragraph 0002). On the other hand, the present invention can identify a genotype of a transgenic mouse and reduce the variability of a transgene expression in the transgenic mouse (see, e.g., paragraph 0004-0006).

As admitted by the Examiner, the present invention has shown that Pol II-Neo transgene (as an example of the transgene of interest) was detected in all mice exhibiting coat color effects.

Thus, one apparent use taught in the specification of the present application regarding the transgenic mice of the present invention is to assist people to visually identify whether the transgene of interest has been expressed based on its color change. In addition, it is apparent that a person of ordinary skill in the art would know different specific use of different mouse with different transgene of interest.

Hence, contrary to the Examiner's assertion, the specification has disclosed how to use the transgenic mouse. The Examiner repeatedly states that "a patentable use" is not provided in the specification. Applicants are not clear about what the Examiner means. 35 U.S.C. 112, first paragraph only requires that the specification disclose how to make and use the claimed invention. No patentable use is required therein. As MPEP 2164.01 (c) states:" If a statement of utility in the specification contains within it a connotation of how to use, and/or the art recognizes that standard of modes of administration are known and contemplated, 35 U.S.C. 112 is satisfied." "When a compound or composition claim is not limited by a recited use, any enabled use that would reasonably correlate with the entire scope of that claim is sufficient to preclude a rejection for nonenablment based on how to use." Emphasis supplied.

In addition, where claims 9 and 12-17 are directed to a transgenic mouse, all the remaining pending claims are directed to either a vector or a method of producing transgenic mouse. The Examiner rejects all the pending claims 9-29 for the same reason that no patentable use of the transgenic mouse is shown. The Examiner does not provide any reasonable basis to support his conclusion.

For example, researchers can use the vector (or construct) of the present invention to insert a transgene of their interest between the coat color cassette and insulators to identify whether the transgene of interest has been expressed in the mouse based on its color change. The same applies to the method of making transgenic mouse.

The Examiner also asserts that expression form Pol II does not provide a mouse that has a use as a disease model (Page 5 of the Office Action). The Examiner comments that the mouse with expression of a neomycin resistance gene from the Pol II promoter has no use. The transgenic mice we generated in examples 1 and 2 were used to demonstrate the effects of our specific constructs on transgene expression. Neomycin resistant gene and eGFP are examples of transgene for analysis. The Pol II promoter was chosen to control the transgene, because it is ubiquitous and easy for analysis. Neomycin resistant gene and eGFP can be replaced by other transgene of interest that needs to be expressed in a mouse (see e.g., paragraphs 15-16 of the specification). The transgenic mice that Applicants demonstrate in the specification are not

expected for use as a disease model. Applicants use these examples to show that the present invention can enhance transgene expression rate and characterize the genotype visually with coat color change. It is apparent from the teaching of the specification that a researcher can establish a disease model with transgenic mouse in accordance with present invention (see e.g., paragraphs 15-16 of the specification). Further, the Examiner does not provide any basis or explanation as to why only disease model can satisfy the enablement requirement under 35 U.S.C. 112, first paragraph. As noted above, one apparent use taught in the specification of the present application regarding the transgenic mice of the present invention is to assist people to visually identify whether the transgene of interest has been expressed based on its color change, regardless of whether it is a disease model.

The Examiner also states the particular expression cassette described in the specification demonstrates a lack of reproducibility (Page 6 of the Office Action). Specifically, the Examiner cites to pages 17, paragraph 3, lines 1-5 and Fig. 1A and notes that the specification discloses eleven founder transgenic mice comprising Ag cDNA operably linked to the K14 promote without the Pol II promoter and chicken β-globulin HS4 insulator and only one of the eleven had a detectable coat color phenotype.

In fact, the construct (A) Ag and (B) AgNeo without chicken insulators were used as the **control groups** to compare the effect of insulators in transgene expression. As disclosed in the specification, the coat color effect of construct (A) Ag and (B) AgNeo without chicken insulators was low. The coat color effect was increased in these constructs containing chicken insulators (fig 1C, D, E, F) in accordance with the present invention. Hence, Applicants do not agree with the Examiner's opinion that the present invention lacks reproducibility based on the low expression rate in **control groups** by conventional transgenic construct rather than by the present invention.

Based on the foregoing, Applicants respectfully request withdrawal of the rejections of claims 9-29.

It is believed that no other fees or charges are required at this time in connection with the present application; however, if any fees or charges are required at this time, they may be charged to our Patent and Trademark Office Deposit Account No. 03-2412.

Respectfully submitted,

COHEN, PONTANI, LIEBERMAN & PAVANE

By _____

Kent H. Cheng
Reg. No. 33,849
551 Fifth Avenue, Suite 1210
New York, New York 10176
(212) 687-2770

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